March 4, 2003

Katherine L. Rhyne
Technical Contact
King & Spalding
1730 Pennsylvania Avenue N.W.
Suite 1100
Washington, DC 20006

Dear Ms. Rhyne:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Melamine, Hexakis (Methoxymethyl)- posted on the ChemRTK HPV Challenge Program Web site on November 4, 2002. I commend The HMMM Coalition for their commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that The HMMM Coalition advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: C. Auer
A. Abramson
W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Hexamethoxymethylmelamine

Summary of EPA Comments

The sponsor, the HMMM Coalition, submitted a test plan and robust summaries to EPA on October 29, 2002 for hexamethoxymethylmelamine (HMMM, CAS No. 3089-11-0). EPA posted the submission on the ChemRTK HPV Challenge Website on November 4, 2002.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties. The data for boiling point, vapor pressure, and partition coefficient are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured data for melting point and water solubility for the commercial product containing the highest amount of HMMM (approximately 50%).

2. Environmental Fate. The data for photodegradation and transport and distribution (fugacity) are adequate for the purposes of the HPV Challenge Program. However, the submitter needs to address deficiencies in the robust summaries. EPA agrees with the submitter's proposal to conduct hydrolysis testing and recommends that the submitter provide measured ready biodegradation data on the commercial product containing the highest amount of HMMM (approximately 50%).

3. Health Effects. EPA reserves judgement on the adequacy of submitted data pending submission of the composition of test materials used in the acute, repeated-dose, and genetic toxicity studies. EPA agrees with the submitter that testing of the commercial product containing 50% HMMM according to OECD Guideline 422 will adequately address the reproduction/developmental endpoints.

4. Ecological Effects. EPA agrees with the submitter's proposal to conduct an algal toxicity test. The submitter needs to specify the composition of the test substance that will be tested. The submitter needs to provide a few missing data elements and detail the composition of the test substance in the robust summaries for fish and daphnia tests.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the Hexamethoxymethylmelamine Challenge Submission

Description of the HPV Substance

a) General. The submitter needs to clarify the nature of the title substance. In particular, the relationship between the "monomeric" and "low molecular weight polymeric" versions is unclear, and whether the designation "HMMM" includes both substances. In addition, the submitter needs to explain whether the percentage of HMMM cited always refers to the monomeric form and whether the nonmonomeric portion is largely dimers and trimers, higher oligomers/polymers or other substances. To the extent possible, the information on the relative quantities of nonmonomeric substances will aid reviewers.

b) Specific. Several data sets were generated using 29 ± 1% hexamethoxymethylmelamine. The submitter needs to define the remaining major components of the tested materials insofar as possible.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The data for boiling point, vapor pressure, and partition coefficient are adequate for the purposes of the HPV challenge Program.

Melting Point. The submitted calculated (EPIWIN) melting point value of 188.4 °C is significantly different from the literature value of 42-55 °C (Beilstein online database). The submitter needs to provide measured melting point data following OECD Guideline 102 for the commercial product containing the highest amount of HMMM (approximately 50%). The use of estimated values introduces uncertainties that then become magnified in modeling applications.

Water Solubility. The submitter's estimated water solubility value of 149.3 mg/L at 25 °C (WSKOW v. 1.40) is greater than the OECD cutoff value of 1 µg/L; therefore, the submitter needs to determine water solubility experimentally according to OECD Guideline 105. [By using the literature melting point value of 49 °C as an input, the water solubility program provides a water solubility of 1980 mg/L, an increase of almost 10-fold.]

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

Photodegradation. The data are adequate for the purposes of the HPV Challenge Program.

Stability in Water. EPA agrees with the submitter's proposal to conduct hydrolysis testing and recommends that the testing be done according to OECD Guideline 111.

Biodegradation. The submitter's BIOWIN-based conclusions as to biodegradability are insufficient. EPA recommends that the submitter provide measured ready biodegradation data following OECD Guideline 301 for the commercial product containing the highest amount of HMMM (approximately 50%).

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

The submitted data for acute, repeated-dose, and genetic toxicity were developed using 29 ± 1% hexamethoxymethylmelamine. However, the submitter did not define the remaining major components (approximately 71%) of the tested material. If, as suggested on page 3 of the test plan, the major components were HMMM and higher oligomers, the data would be acceptable and no further testing would be needed for these endpoints, since the oligomers would likely be less toxic than the monomer HMMM. However, if the other components are less methylolated/methylated species, then the toxicity of the non-HMMM components related to HMMM is less certain. Therefore, EPA reserves judgement on data adequacy until a better description of the test material composition is available.

The submitter has indicated that it will conduct a combined reproductive and developmental toxicity testing "using the OECD guideline 422." OECD guideline 422 is actually a screening test for combined repeated-dose/reproductive/developmental toxicity; however, EPA believes that the OECD 422 screen is the appropriate test because then all three interrelated systemic toxicity endpoints will be tested by the same route of administration (oral) and with no increase in the number of animals.

Ecological Effects (fish, invertebrates, and algae)

Fish and invertebrates: Adequate data are available for the purposes of the HPV Challenge Program. The submitter needs to include information missing from the robust summaries.

Algae: EPA agrees with submitter's proposal to conduct an algal toxicity test. However, the submitter needs to identify the composition of the intended test substance.

Specific Comments on the Robust Summaries

Environmental Fate

Transport and Distribution (fugacity). The submitter needs to incorporate in the robust summary the values of the input parameters used in the model.

Health Effects

Although all submitted robust summaries were excellent, none of the summaries adequately identified the test material. For all studies, summaries need to identify as clearly as possible the residual material in the tested product to enable an adequate evaluation of the studies.

Ecological Effects

Fish and Invertebrates. The submitter needs to provide the following information as appropriate: commercial test substance composition, water hardness, temperature, pH, dissolved oxygen, and the amount of solvent (acetone) used in the key studies.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.